INTELLECTUAL PROPERTY AND THE ENTREPRENEURIAL ACADEME

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~~~ *Everything Flows*. Heraclitus ~~~

ABSTRACT

The growth of commercially funded research and development (R&D) is thzreatening scientific integrity, especially in clinical research into new drugs, some of which rests on confusions about intellectual property. To sort out these questions I will first explore the dynamics of the (scientific) research, (technological) innovation, and (product) development continuum. The openness ethic implicit in scientific research is requires a common intellectual property right; but research today is often performed by university / business partnerships. Commercial technology and product development, in contrast to scientific research calls for a private property approach, e.g., in pharmaceutical R&D. studies of possible bias toward positive findings in commercially funded clinical research however reinforces the concerns raised by several recent cases in which scientific values clashed with the commercial demands (the Olivieri, Gelsinger and Dong cases). Nonetheless a solution space can be opened up by using the R, T & D continuum to sort out the different modes of intellectual property rights demanded by the competing interests of researchers and firms. While the focus is on the pharmaceutical sector, much of the argument applies to other high tech industries, like electronics, chemicals, aerospace, etc.

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> Science is the raw material that applied research and engineering refine into their products, [but] scientific research is by nature an uncertain undertaking.
>
> Nathan Myhrvold. Vice President, Microsoft.[1]

> Medical innovation depends on the extensive interactions between universities and industry , with knowledge and technology transfer flowing in both directions. Important roles and obligations on both sides have been neglected.
>
> Gelijns and Thier, 2002.

THE QUESTION

Research is not only uncertain, as Nathan Myhrvold cautions, it is also costly. Furthermore technological innovation is increasingly involved in a scientific inquiry; and new technologies often have significant Market potential. Commercial interest is especially strong in electronic telecommunications and pharmaceutical R&D. This may involve significant risks to scientific integrity, partly because of confusions about the nature of intellectual property rights. Using a model of the R&D continuum that shows complex links between scientific research, technological innovation and commercial product development, this paper seeks to clarify the intellectual property issue, by noting the competing interests involved in commercially funded clinical trials of new drugs. On that basis I will suggest a triage type, multi-levelled solution to the problem that recognizes the legitimate claims of all the stakeholders involved, patients, scientists, universities, and businesses.

Two assumptions need stating, from the first. First, since scientific research is a human project, it is not deemed 'value neutral.' Rather all knowledges are seen as part of social life, and therefore as serving human purposes and interests (Dewey, ? ; Peirce, ? ;Habermas, 1971). Assuredly, knowledge is useful to life, e.g., more than ignorance or error. Even number theory is relevant to coding and cryptography. Given the usefulness of knowledge, transfering what we learn about the world, tre.g., through scientific research, into useful technologies and products is to be expected.

The question here is not whether scientific research interacts with other human projects and interests, but how, and to what effect, especially in the case of commercially funded clinical research into new pharmaceuticals.

A high tech knowledge economy then is not a surprise, but a simple corollary of the usefulness of knowledge. But it has its dangers. An important challenge it faces is how to change the present socio-economic institution of research so as to both protect commercially sensitive information 'while at the same time ensuring that research findings and their implications are available to the public and the scientific community." (La Montagne, 2001: 1724).

Here we confront a core tension in the high tech knowledge economy: between researchers freely pursing knowledge, patients seeking effective, safe treatments, and firms seeking new products and returns on their investments (Gelijns & Thier, 2002: 75) conflicting intellectual property rights involved when the research is commercially funded, viz., between scientific openness and private intellectual property.

Second, scientific research is not free. It involves work by individual researchers, and therefore intellectual property rights. New ground rules are needed to guide all parties and institutions involved, academic, business in the complex process of R&D in the contemporary high tech knowledge economy. Sorting out the ground rules for intellectual property is the main aim of this paper.

TRANSLATIONAL RESEARCH

Translational research involves the productive application of the overlapping assets of industry and academic laboratories" making collaboration between university and business 'very fruitful.' (Geljins and Their, 2002). As in Merck / UBC partnerships in Alzheimer's treatment research (Marron, 1998).

It denotes "the conversion of an idea into some practical (useful) product", and this reveals 'a major potential pitfall related to …intellectual property.' (Vallance, 2001: 1804). It covers a variety of "interrelated and interdependent steps… from concept to clinical application, and from discovery to dissemination, translating novel scientific insights into new approaches for prevention, diagnosis and treatment of disease." (Fontanarosa, et al. 2001). from basic science to clinical investigation.

Most pharmaceutical R&D however seems to span the transition from scientific research to technological innovation and product development. 33% of pharmaceutical industry R&D is geared to "applied research", defined as "including investigations directed toward discovery of new scientific knowledge that has specific commercial objectives" (PhRMA, 2000; cf. Lancet, 1999a). 67% of pharmaceutical industry R&D is allocated to "development", i.e., "technical activities related to translating research findings into products" (T1 to D3?). Over 80% of that is allocated to developing new products, and 18.4 % to modifying existing products (D1 to D3; PhRMA, 2000). Then there is support of "translational research", into "disease mechanisms and processes that become the target of pharmaceutical (i.e., technological) intervention." Phase I clinical trials for instance may involve new technologies, some of which 'apply' recent scientific research (R2 to T1). Phase II trials roughly correlate with modifying existing technologies and developing manufacturing prototypes (T2-D1), Phase III with further product development (D2), and Phase IV involves drugs already on the market (D3).

Institutional interdependence and partnerships, not independence, are the norm in contemporary 'translational' research, the final step from the research lab to the clinic (La Montagne, 2001). The impressive growth of the bio technology industry over the last decade has been due to growth in scientific knowledge, government support of basic research, increased private investment, and the success of some biotech products (La Montagne, 2001).

The oversight responsibility for translational research is however diffused, among academics, universities, and funding partners, public and private. It involves latent tensions, such as divided loyalties for researchers and host institutions, especially in biomedical and clinical research (Lancet, 1999a; Polanyi, 1999; Stornberg 2000; Nichols and Skooglund, 1998).

Technologies represent material assets (in the Einsteinian sense which includes radio-electronic and other forms of energy as well as physical mechanisms and masses; see Stefik, 393f). This is where an intellectual property problem arises.

The R (T) & D CONTINUUM – COGNITIVE COMPLEXITY

Reality is messier than any neat and tidy theory or mathematical model suggests. This is especially true of R&D, and even more so in clinical research. Scientific research is part of a long, complex R&D continuum. It stretches from fundamental scientific inquiry to technological innovation and culminates in commercial product development (cf. Freeman, 1986, Freeman and Soete, 1997; Kuhn, 1963). It is both cognitively and socially complex, involving diverse knowledges and institutions (cf Gelijns and Their, 2002: 75; di Norcia, 2002). To clarify this process, and following common practice (see Buderi, 2000a: ch. 1), I have divided R&D into three phases: scientific research, technological innovation, and product development, each with three stages, as shown in Table 1.

Table 1	**THE R&D CONTINUUM**		
R&D PHASES	**RADICAL INNOVATION STAGE**	**ARTICULATION STAGE**	**REFINEMENT STAGE**
R SCIENTIFIC RESEARCH PHASE	R1 Paradigm Shift Research	R2 Paradigm Articulation	R3 Routine Research
T TECHNOLOGICAL DEVELOPMENT PHASE	T1 Radically New Inventions	T2 Major Improvements	T3 Adjustments & Imitations
D PRODUCT DEVELOPMENT PHASE	D1 Manufacturing Prototypes	D2 Production Models	D3 Market Models

Because of the complexity indicated in the above table, ‘R&D’ in this paper will denote the three fold, R, T & D continuum, unless otherwise indicated.

The R, T & D continuum helps us to sort out the uncertainties and ambiguities of ‘translational research’ in medicine. First, it is important to note that the radical innovation stage is far more fraught with uncertainty than routine research or development. Thus scientists dealing with revolutionary new paradigms (R1), inventors of radically new technologies and entrepreneurial product developers, all are involved in making choices in an environment replete with great promise, and risk, in contrast to the routine work (R3, T3, and D3) stages of refining well established findings, technologies or products. In the early (R1, T1, and D1) highly innovative, and creative stages, less is known and more is uncertain. Whether they are scientists, inventors or entrepreneurs, they are gambling a that their time, resources, efforts and

(somebody's) money on a long odds bet that the cognitive, technical and economic benefits of their enterprise will outweigh the risks.

Secondly, while there is a lot of discussion about research and development, the critical, mediating role of technological innovation, 'T' is a separate, autonomous phase in R&D, technological innovation. IT differs from both scientific research and commercial product development. Technological innovation is quite distinct from both scientific research and from commercial product development, both in its inherent dynamic, practices and in its ethos. Thus authors and discoverers of new knowledge are not identical with inventors of new technologies (Ducor, 2000). The T in R, T & D, is often unnoticed and its significance neglected. The commercialization of scientific research, I would suggest, almost always involves technological innovation, and this has serious intellectual property implications, as will be indicated below.

But science is an uncertain, exploratory process, and even the best researchers make errors. No one can predict what a research project will find or how useful it might be (Myhrvold, 1998). The more radical and fundamental the research, the longer it takes to pursue and the less predictable its benefits: e.g., 50 years for both nuclear energy and genetics. In consequence it should be open rather than proprietary. Indeed it is in gene therapy research that the tragic, and death of a young volunteer research subject, Jesse Gelsinger occurred,, due to inadequate safety protections.

The R, T & D continuum is interactive, not linear, expressing the complex interactions among the host institutions supporting R&D: universities, hospitals, healthcare professions, government agencies, and, increasingly, businesses. in biotechnology for example academic research "catalyzed basic research in the pharmaceutical industry" notably in molecular biology (Geljins and Their, 2002; cf Buderi, 2000a). R, T&D is multidirectional, and interactive, not siloed or linear. This interaction underlies the development of new healthcare products (Gelijjns and Thier, 2002).

RESEARCH : Verifying hypotheses occurs in the scientific research phase, while clinical testing of a new pharmaceutical assumes that a variety of bacterial or genetic technologies essential to their manufacturer have been developed, and that, if and when the clinical trials are successful a commercially viable product can be developed. Biomedical scientific research is itself complex; it can be divided into three types: basic research, disease and patient oriented (or clinical) research (Rees, 2000). In some cases, such as the Dong and Olivieri cases, the 'technology', the new drug, is already invented. This does not imply that further scientific research is not needed. Both Betty Dong and Nancy Olivieri were pursuing the scientific testing required to ensure that new drugs were what they at first promised to be. Scientific research is not a simple, solitary matter, but a collaborative social process, e.g, within the research team, including technicians as well as investigators, and publication involves "authors, peer reviewers, editors, granting agencies, universities" etc (CMAJ-CIRH, 2001).

TECHNOLOGY : The transition / transfer of scientific research into technological innovation, or technology transfer within the R, T & D continuum is a locus of much of the tension in translational research, especially when it is commercially funded. The cognitive complexity of the R,T & D continuum hints at its social complexity. Many groups are involved in the process from an insight / hypothesis to its technological innovation, and finally its

introduction as a new product in a market. Clinical trials often involve exchanges among diverse knowledges: physical, chemical, biological sciences, computer modelling and data crunching, engineering type technical design and testing skills (G&Thiers, 2002). Once knowledge has taken useful, material embodiment in a useful technology however it is a harder 'real' asset, the kind of entity for which private (intellectual) property is applicable (T1 and T2).

Increasingly, scientific knowledge not only enters the culture's stock of knowledge but is also translated into a factor of production. Marconi's 1896 patent application for his long range radio transmitter was a translation of Maxwell's theory of the electromagnetic field into a technological innovation (Etzkowitz, 2001: 23). It typified a now classic path through the R, T & D continuum in the knowledge economy, from research through technology to the marketplace, in which Intellectual property is assumed, mistakenly, to refer to the application of private property to cognitive goods like information, research results, knowledge, etc (cf La Montagne, 2001: 1724). And today scientific research involves numerous innovative technologies, e.g., electronic microscopes computerized databases and modelling systems, special chemicals, etc.

Countless technologies are involved in healthcare: from stethoscopes, thermometers, bandages, and needles to drugs, PETScans / MRI imaging and, computerized tomography (Zeidenberg, 2002b), pacemakers, and defribillators (Jeffrey, 2001), endoscopy diagnostic aids, to surgical devices such as knives, sutures, and sterilization, etc. That technological complexity echoes the cognitive complexity of scientific research.

The Human Genome Project exemplifes the growing integration of scientific research and computer technologies. Computer databases and modeling is involved e.g., in gene mapping, sequencing and their ultimate application in developing new gene therapies, for most illnesses have hereditary components (Collins and McKusick, 2001). Computerization is facilitating the operation of healthcare databases, networks, and operating telehealth distance technologies, e.g., for surgery in remote communities (Zeidenberg, J. 2002a). Their testing and improvement involves extensive activity in the technological innovation phase of R T &D, and is especially involved in the evolution of genetic medicine, from the basic science of the Human Genome Project, to developing gene therapies e.g. for cystic fibrosis, cancer and many other conditions, to the development of new commercial pharmaceuticals (Kaji and Leiden, 2001; Bumol and Watanabe, 2001; Nathan, et al, 2001).

Genetic medicine is high tech in all stages of its development, from mapping and sequencing genes and identifying their the dynamics of their interactions with molecular partners such as proteins, and their roles in the aetiology of diverse diseases (Pollard, 2002). Complex proteonomics and their potentials for new therapies, and genetic research could not be done without electron microscopes, esoteric procedures in molecular biology, and extensive computer based mathematical modeling (Echols, 2001; Pollard, 2002).

D: PRODUCT DEVELOPMENT: Bringing new technologies to market involves development costs. Manufacturing prototypes (D1) need redesigning to be produced in volume (D2) and made suitable for sale to / use by consumers (D3). As one moves from research to technological innovation and then to product development, the appropriate intellectual property regime shifts from a common to a private property right.

The RT&D continuum is interactive and dynamic. It is not a linear development through several stages in a preprogrammed sequence (e.g., as with a seed or embryo). Work in each, relatively distinct, scientific, technological, and development phase often affects that in the others. New technologies like computers have for example affected the direction and potential of scientific research, just as market demands have influenced technology design. The transition from routine research (R3) to technological innovation (T1, T2), is an especially gray area. In it scientific discoveries of how nature functions bleed into new technologies, and new technologies enable new research, e.g., as in the case of the microscope and the computer.

SCIENTIFIC OPENNESS & (COMMON) INTELLECTUAL PROPERTY

It is a very clear moral issue. S A Rosenberg of Nl Cancer institute says, If youwithold information you potentially delay progress. If you delay progress you potentially delay the development of effective treatments, and human beings suffer and die who need not have don so (in Gibbs, 1996). Open communication is needed between scientific investigators and technical innovators: The evolution of technology, Geliins and Their write,"requires lines of communication that allow information to flow freely from clinicians back to the research enterprise, both in academia and industry', and I would add, teaching hospitals, and appropriate government regulatory agencies (2002).

"Only in science", S. J. Garte contends, "is the complete, unmodified, and total truth... the sole necessary and sufficient yardstick of achievement" (Garte, 59). The open publication of and full access to hypotheses, methods, data, and findings, especially to the appropriate knowledge community, is a core ethical imperative in scientific research (Munthe and Welin, 1996; Pearn, 1995; Wise and Drury, 1996; Lancet, 1999b). Without their publication researchers can not "scrutinise the methods, analysis and conclusions, and attempt to replicate the findings" of a project (Roy, 1999; cf Lederberg, in Stefik,).

'Scientists want full disclosure of research results as soon as possible' subject to peer review.' (La Montagne, 2001: 1724). Open communication of ideas is fundamental to the scientific culture (Martin, 2000). Sometimes an idea is so practical that merely trying it proves its validity at once, such as the stirrup or the outrigger on a canoe. The idea of vaccination was one of the historical advances in medicine; similarly the usefulness of nitric oxide patches in treating angina. A gynaecologist saw the potential for nitric oxide for inhibiting premature labour. Ideas need open discussion, as well as experimental testing; but without the idea, the experiment is not possible.

Scientific integrity then assumes openness, the unrestricted communication of, access to, full information about a research project, not just its results and methods, but its design and data. This powerful bias for complete openness is the core value in the scientific ethos, its way of giving concrete form to the core moral value of open and honest communication; and that ethos is the value system that drives the research phase of the R, T & D continuum (see di Norcia, 1998: 4f).

This implies a research ethic, e.g., of avoiding undue influences in seeking the truth. In this sense "good science is ethical science" (Garte, 60f). And the core communication value of openness is central to the knowledge economy; for, as Sheila Frame, an AstraZeneca VP, notes:

"The spirit of scientific debate has a long history of supporting independent peer reviewed research that leads to beneficial products" (in Shuchman, 1999b). And openness is common in the internet economy, for instance, in developing new systems, e.g., open source software like Linux, and giving browser software away, as with Netscape (Berners-Lee).

Openness is also the default value in human communication. Words and concepts are intrinsically communicable. They are by nature messages more than data. A private language is a contradiction in terms, and privacy is a relatively new social norm. Conversation and ideas furthermore are free goods. They may not be copyrighted or patented. While scientific research is not casual conversation, it is not (and cannot be) the private work of a solitary unaided mind. On the contrary, science is committed to openness and transparency, to full disclosure of research data, methods and findings, and the encouragement of wide ranging debate. The claim of research findings to the status of knowledge requires not only objective evidence, but also transparent communication of that evidence and independent (and successful) testing and replication of findings by one's peers (polanyi, 1999). A necessary condition of transforming research ideas and hypotheses into knowledge then requires openness. Prior to the 20th century knowledge explosion, true, most research involved armchair reflection or literary diversion by amateurs. Such individuals were usually people of relatively independent means like Charles Darwin, or a monk supported by the church, like Gregor Mendel. Nonetheless science typically involves a collaborative, lengthy, and increasingly technological and costly enterprise (Kuhn, 1965; Freeman and Soete, 1997). And the sciences have now evolved into so many species of knowledge that no individual can hope to know everything, as Leibniz once presumed. Scientific research furthermore

CLINICAL RESEARCH

The openness ethic is an especially acute concern in clinical research. While patient safety comes first, the earlier and newer the research, as was noted before, the greater the uncertainty about data and evidence. Difficult Judgement calls on patient risk sometimes have to be made by the researchers, notably where some early adverse findings arise, but it is too early to explain them and discriminate whether they reflect random variation, and do not therefore imply that the therapy under study is unsafe or inefficacious, Thus, "the decisions to stop a clinical trial is complex and must incorporate information on adverse events and clinically relevant outcomes." (Becker and Tirschwell, 2001) Balancing the duties of minimizing patient risk with the pursuit of research into promising hypotheses, can lead to difficult ethical tensions in clinical research. They can be exacerbated by unrealistic, and all too naturally hopeful, expectations of great benefits from early, small clinical trials of promising new therapies and treatments—for they exemplify new technologies. Thus the reliable assessment of the effects of new drugs requires impartial, appropriately randomised trials and research free of bias. And without reliable assessment may lead, as it has in the past to unnecessary suffering and even death (Collins and McMahon, 2001).

Over the last 25 years the number of clinical trials has doubled, and of patients, tripled (PhRMA, 2000). And clinical trials can be a costly investment. A new drug takes on average 14.2 years to develop (up from 8.1 in the 1960s), but only 3 out of 10 approved drugs recovered their R&D costs. The pharmaceutical industry however is quite healthy. In 1999, the *Fortune* 1000 index says, the top twelve US pharmaceutical firms made an average profit rate of about

17% on revenues, which were up by 12.3% over 1998. Sales of the top five firms, averaged $8.3 billion, while the average cost of a prescription in the U.S. went from $23.68 in 1991 to $37.38 in 1998, a 58% increase. The industry spent $13.9 billion to spend on promoting its products, up from $9.2 billion in 1996.

As the number, size and costs of clinical research projects increase, the commercial funding of clinical trials is becoming more common, e.g., by pharmaceutical companies. Phase I trials are designed to determine safety and dosage (NIH, 2000). They usually involve a few normal, healthy subjects and, take a few months. Phase II trials, which test for efficacy, may involve 200 to 300 patient volunteers, and take up to two years. Phase III, Pilot Project trials, are designed to confirm efficacy. Typically, they involve 1000-3000 subjects and last three years. Finally Phase IV trials represent the Post Marketing Evaluation of drugs in general use by physicians, and may take several more years.

Competing interests may influence research design. The research may for instance test a new drug against competing treatments--as in the Dong case--, against a control group, or a placebo. Whatever the case, there should be clarity about what counts as favourable or unfavourable results--e.g., evidence for / against safety and efficacy (as in the Olivieri case), quantitative (sample size) and qualitative (medical condition) criteria for including subjects, adequate informed consent provisions (as in the Gelsinger case), cost recovery and financial returns concerns of the funding agency, etc (Brody, 407ff; Huth, 398f). Jesse Gelsinger's death in a clinical trials of a new gene therapy setback the research and led to FDA sanctions on host institutions like universities as well as drug companies, (Vogel, 2000a, 2000b; Gura, 2001).

What is central in all these cases is the principle of academic freedom, as a *The Olivieri Report* and many others have argued (*The Olivieri Report*, 2001: ; N&W 2002: 1369-70). Clinical trials should be undertaken only if they are scientifically sound and conducted by competent researchers (Huth, 1996: 400f). Open publication of the complete results of clinical trials, *the Lancet* argues, is a prerequisite to discussions of safety and efficacy (Editorial, 1999b). Biased research moreover can threaten patient health as well as violate the integrity of science.

Pharmaceutical firms should make available all clinical research data, about adverse as well as beneficial effects, and about the ineffectiveness as well as efficacy of new drugs (Roberts, Wan Po and Chambers, 1998). All clinical trials should therefore be registered and their results be published, so that the fullest sample of information is available to all researchers (Tonks, 1999; Roy, 1999). Pharmaceutical firms do not always succed in blocking publication of adverse findings, as Merck Sharpe and Dohme found in the Norwegian courts in 1997 (Goldbeck-Wood, BMJ 1997)

In addition to openness, clinical research also has an obligation of care for the health of patients / subjects under study, and to seek their informed consent to the research. Hence clinical research operates under the guidance of an independent Research Ethics Committee, usually in a teaching hospital (see Kurt, 386; Huth, 402f; but patient health and informed consent issues are not the focus of this paper). Subjects consent to research is motivated by the understanding that the research can help future patients. Thus they implicitly support the public dissemination of

the knowledge gained, and a common intellectual property in research (H. Mann, 1999). Commercial funding may however conflict with the openness ethic, as some recent cases show.

Secretiveness in research, however, can cost lives. In the 1980s for example a partnership between government agencies and pharmaceutical firms led to problems over the safety of the blood supply. Plasma was prepared by pooling blood from thousands of blood donors across the USA, many of whom were infected with HIV or Hepatitis (Shimm, Spece, and DiGregorio, 1996). Even though they were then the largest AIDs infected group homosexuals, and prisoners were not excluded as donors, because of privacy concerns. The old 'coagulate factor concentrate' manufacturers tried to convince MDs that the infection risk was small, lobbied the government to delay general implementation of the Hepatitis B core antibody test for donors, and resisted shifting to using a safer 'cryoprecipitate' product for hemophiliacs. As a result many physicians and patients, notably hemophiliacs, were not warned of the critical health risks involved in using the tainted plasma. Known preventive measures were not taken. These problems led Thomas Drees, CEO of Alpha Therapeutics, to charge his competitors with conspiring to avoid using the Hep B test. If it "had been used from 1975," he claimed, "countless deaths from Hepatitis B .... would have been avoided. Further, thousands of hemophiliacs would not have AIDS today (Shimm, Spece, and DiGregorio, 341). (Drees was later fired, he alleged, for taking these actions)

According to the US Pharmaceutical Manufacturers Association (or PhRMA), 28.3% of pharmaceutical industry R&D goes to Phase I to III trials, 5.8% to Phase IV, and 9.9% to process technology and quality control. Success can mean millions in revenue for pharmaceutical firms, but high returns are the exception rather than the rule (*Lancet* editorial, 1996). Indeed, "the interpretation of data from clinical trials can be a difficult and contentious business", as a 1996 *Lancet* editorial comments; so "researchers should not be "harangued for practising good clinical research, and patients have a right to unbiased, complete research findings" *(*Editorial, 1996). Where trial populations are small and the drugs costly, even a successful trial can sometimes be a net cost to the funding firm. Nonetheless, PhRMA notes, findings that advance scientific knowledge often emerge, viz., about a drug's safety and efficacy.

IP TENSIONS in COMMERCIALLY FUNDED RESEARCH

Research is intellectual work, it needs economic and financial support (Rees, 2000). It is not a free good. Hence the importance of funding, public and private and of intellectual property rights protections. Researchers need to be compensated. Great scientists like Louis Pasteur and Albert Einstein for instance received an income from public institutions; and academic researchers are usually salaried and tenured. Being financially secure, they can focus their interest on discovering the truth, rather than on making money, e.g., by selling technological innovations or commercial products (cf. Shimm and Spece, 370). But the more extensive, complex and difficult a R&D project, the more resources it needs. Research related information should therefore be treated as intellectual property, so that its publication and the researchers' intellectual work can be appropriately recognized and rewarded. One should certainly not suffer losses for doing research. Host institutions like universities, and funding sponsors should also share in any returns from any resulting patents or products, so as to recover their costs and, if possible, reap a return on their investments.

There has been a massive shift in research funding from public to private sector, (Gibbs, 1996), Commercial funding involves a proprietary or private intellectual property regime (Smith, 1994, 1998; Angell, 1996; Huth, 390; Horton, 1997; Franck, 1997). A 1994 Carnegie Mellon survey reported that 82% of life science firms (biotech, genetics and pharmaceuticals), require scientists to keep results confidential for months, so as to facilitate patent filing (Whitbeck, 297). 35% of the scientists surveyed had signed agreements allowing sponsors to delete information from publications. 53% agreed to publication delays (usually less than a year), mostly to give funding organizations a head start in developing a commercial product.

This raises the Lancet's editor's question in 2002, 'How tainted by commercial conflicts has medicine become?" (Editorial, April 2002; Martin and Kasper, 2000). Commercial funding involves research tensions: decreasing openness in communication, bias in reporting research results, and choices about the type of research conducted, financial incentives for both researchers and patients in clinical research, and conflicting interests (Gelijns and Thier, 2002).

Businesses operate under short term time pressures, so they cannot afford to be patient. The best way to get research funding may be to predict the results up front, guarantee low risk of failure and offer a clear path from research to product development and profit (Myhrvold, 1998). Over-reliance on commercial funding however may not only narrow the research horizon but also bias researchers against negative results.

This also happens with government funded research, viz., for nuclear energy and weaponry. Financial interests may lead researchers to overstate the efficacy of a company's drugs and urge their premature licencing (Ferriman, 1999). Commercial pressures, a *Lancet* reports, have led to interference with independently run clinical trials, the *Lancet* argues (editorial, 1997). There are also concerns about misleadingly positive advertising and drug promotion information.

In commercially funded research, as one moves closer to translating new technologies into products manufactured for markets, the research findings tend to be treated as the private property of the sponsor firm, rather than the common intellectual property of the scientific community. Several intellectual property problems are in addition raised by commercially funded research: secrecy, intimidation of researchers, limiting scientific communication, biased interpretation of data and findings, diversion of university resources to applied, shifting the research agenda away from scientific questions toward applied technology and commercial products, etc. (Huth, 1996; Garte, 1995). The intimidation of researchers and threats of litigation are clearly incompatible with the openness ethic (Deyo, et al., 1997). Indeed the legalization of debates about publishing research data, methods, and findings, transforms them into inappropriate adversarial contests among court 'experts' tends to promote 'junk science' (Huber, 1991). Such debates are more appropriately, and effectively (in terms of verification), aired in the appropriate research community (cf. Munthe and Welin, 1996; Malmesbury, 2000). To clarify the underlying problems it would be better to treat the different stakeholders in scientific research as competing interests.

As several cases show, researchers have divided loyalties—to their patients and their profession, to the research, and to the organizations sponsoring the research. Confusing those responsibilities can have tragic consequences, as the Gelsinger case showed. Thus it is

imperative that we clarify the distinct phases of the R&D continuum, and the diverse interests and rights, especially in intellectual property, that they imply.

Collaboration has its obligations. All the host institutions supporting research, universities, teaching hospitals, and funding sponsors, public and private, are accountable for minimizing health risks to the human subjects of the research and for ensuring the integrity of research. But the tendency to place commercial imperatives above medical ethics, scientific integrity, and academic freedom raises questions about the ability of the host institutions and commercial sponsors of clinical research to live up to their responsibilities [Angell, 2000; *Lancet.* Editorial. (2001) 357: 1141; *Lancet.* Editorial. (2002) Just how tainted has medicine become? *Lancet.* 359: 1167; Moynihan, Heath and Henry, 2002)

This has special relevance to physicians who are clinical researchers and whose project is commercially funded. Clinical research involves the medical professional's obligations to protect the health of the patient / subjects of the research, a subject already well commented on (cf Steinbrook, 2002); (but this concern is not the main focus of the present paper).

One might provisionally locate each of these cases discussed along the R&D continuum. The Gelsinger case involves the relatively new science of genetic therapy (R2). The Holbrook and Olivieri cases represent normal scientific research with commercial potential (R3?). The latter also involved modifying the treatment delivery technology (T2), viz from intravenous to pills. Two cases involved pharmaceuticals firms attempting to suppress findings about the bio-equivalence of brand name and generics (D3), e.g., re Betty Dong's—research contract with Boots--on its top selling hypothyroid treatment Synthroid, and Ann Holbrook's work—for the Ontario Ministry of Health-- on AstraZeneca's ulcer medication , an area in which there seems to be risk of bias for the sponsor's drug over the competitor's (Rennie, 2000; Shuchman, 1999a, 1999b). In R&D terms new drugs are technologies, usually developed within a medical technology network. They are part of larger treatment tool systems, embedded in complex Technology Networks, which interlink researchers, funding organizations and host institutions and interconnect technologies, knowledges, techniques, and treatments, viz., for thalassemia, cancer, heart disease, etc.

In contrast to public funding, which reinforces the scientific ethos of openness, private support tends to favour selective disclosure and private intellectual property right protection notably in the form of patents (La Montdagne, 2001).

The trend to commercial sponsorship by pharmaceutical companies of clinical research is reinforcing concerns about research integrity [ORI, 2001; Lancet Editorial, 2001; Lancet, 2002a) The next step; CMAJ-CIHR (*2001)* Publication Ethics]. Academia and industry, the Lancet editorializes, are increasingly uneasy bedfellows, for "The whole ethos of the biomedical research community is changing," Sir David Weatherall [2000: 355: 1174] feels [cf Kassirer]. There is growing evidence of sponsor bias and interference in the communication of adverse findings [B. Djulbegovic, 2000l Kjaegaard, 2002] Nor is public funding without its problems, for government sponsors may not favour openness but may require classified research, because of their security concerns. As President of Stanford University, Donald Kennedy, had for instance declined to accept secret government military research contracts.[DKennedy. (2002; Malakoff, 2002). Government, political and social ideologies, as well as commercial interest

can, and do, bias research; the point is that the quality of scientific research should be judged on its own merits, and that all interests should be disclosed (Hannum, 1998).

Such problems pose a critical question: Should "licensing authorities and pharmaceutical companies be permitted to licence and market a drug… without making available all the evidence about the beneficial and adverse effects of the drug." (I. Roberts, A. Li Wan Po, I. Chambers, 1998). In reply Donald Kennedy, now the editor of *Science Magazine*, notes that the scientific ethos is incompatible with secrecy and the suppression of research, a principle vigorously supported by; for, he has written, "Scientific culture is by nature oriented to disclosure [and] evaluation by others." (Donald Kennedy. (2000) Secrecy and science).

Scientific research moreover is a distinct form of intellectual rather than commercial work (Buderi, 2000a: 42f). So the private intellectual property right commerce preferred in business is inappropriate to scientific research. Cognitive assets like research related information moreover are not physical goods (or purely mental, for that matter). Rather they are symbolically encoded, communicable cognitive goods. Their cognitive value is moreover reinforced and enhanced by being communicated, for "bad research helps nobody" (Buderi, 2000a: 45). Communication should therefore be facilitated, while access barriers and administrative costs should be minimized (Munthe and Welin, 1996; Whitbeck, 300). Therefore openness and a common intellectual property right are appropriate values, not private property (Negroponte, 47; Lancet, 1999b). In this scientific research resembles communication media like mail, phones, email and the internet (Rowland, 1999; Berners-Lee, 1999).

The need for funding does not moreover imply that the cognitive assets produced by research are anyone's private intellectual property. For one thing, the knowledge workers produce the assets, not the funding organizations. Where, however, commercially funded R&D enables technological innovation and product development, e.g., of new drugs a private intellectual property right may seem appropriate. The tensions between competing common and private intellectual property rights however are evident in several cases of research into pharmaceuticals.

PRIVATE INTELLECTUAL PROPERTY

Modern legal systems usually give companies like pharmaceutical firms several ways of benefiting from their private intellectual property and R&D, notably patents, copyright and TM; I will focus on patents.

A private intellectual property right is however inappropriate in the scientific phase of the R&D continuum. It inhibits the open communication required for research to be fully debated, tested, and proven or disproved. But funding is needed to sustain upstream scientific research (R1 to R3), as well as downstream technology and product development (T1 to D3). The growing reliance on private intellectual property to support scientific research in the knowledge economy may however result in a tragedy of the "anti-commons", in which people underuse resources because too many private owners are excluding others from access to them (Heller and Eisenberg, 1998).

Unfortunately the default assumption, based on legal conventions, is that intellectual property is merely a sub-species of private property. This is a major, critical error, as exploration of the transcendent R, T & D continuum has indicated. Research has costs; and they need to be met. How meeting those costs affect the requirement for it is not only assumed that research inquiry must be open, but also needs to be compensated. Research work involves an intellectual property right; and researchers should be rewarded, but the data, e.g., in the HGP, should be publicly disseminated (Rowen, et al, 2000).

The growth of commercially funded research and development (R&D) is presenting problems about intellectual property in the high tech knowledge economy. After explaining this question the paper explores several cases of commercially funded R&D into new drugs. Scientific openness, or "the unfettered right to publish" one's research. It clashes with the need of drug companies "to suppress, spin, and obfuscate findings that do not suit their commercial purposes", and to interpret the data, write the report and even ghost write the article (Lancet, 2001). The question then arises, whose article is it? (Larkin, 1999) Commercial sponsors of research rarely recognize the right of investigators to publish their results irrespective of the sponsor's views" Their sense of a right to do so rests on assuming a private intellectual property right, and the need to patent the new medical technology / product. That assumption is the default presupposition of most modern legal systems. But scientific research demands openness, not suppression. So it requires a common intellectual property right in contrast to the private property approach preferred in commercial product development.

Applying common property rights appropriate to mobile, fluid resources like fisheries, water and information to information has however been little remarked. [Ostrom, 1990). With the help of a model of the R&D continuum from scientific research to product development, it is then suggested where a common and private intellectual property rights are appropriate. Linking these modes of intellectual property with the diverse interests involved in R&D, I conclude, opens up a rich space for resolving their competition and potential clash. While the focus is on the pharmaceutical sector, much of the argument applies to other high tech industries, like electronics, chemicals, aerospace, etc.

PHARMACEUTICAL RT&D & PATENTS

The drive to patent new pharmaceuticals underlies the tensions in the Dong, Gelsinger and Olivieri cases. The law's presupposition of private property in intellectual goods is a central source of the tension between legal and scientific / healthcare notions of openness, communication, research ethics. Resolving this 'clash of cultures' and ethics is a main concern of this paper (cf. Lancet, 2002b; Goldner 1998). Pharmaceuticals are a leading sector in the high tech economy, as the TR Patent and R&D scorecards suggests (see Table 2). While pharmaceutical firms may lag behind the high tech pack in the number of patents issued and in innovation speed (which may be due to the length of R&D and clinical research needed for new drugs), they gained top marks for the number of links to scientific research in their patents.

TABLE 2: TR R&D SCORECARD (TOP 10	**SCIENCE LINKS**	**NUMBER OF**	**R&D AS % OF**

FIRMS, 2000) INDUSTRY	(AVERAGE # OF REFERENCES IN PATENT)	PATENTS	REVENUE
AEROSPACE	0.86	143.6	4.9
AUTOMOTIVE	0.33	401.3	5.3
CHEMICAL	3.74	349.6	5.9
COMPUTER	1.1	1018.7	8.0
ELECTRONIC	0.49	1072.2	8.1
PHARMACEUTICAL	8.02	191.3	15.7
SEMICONDUCTOR	1.2	460.8	16.1
TELECOMMUNICATIONS	0.97	483.7	13.5
SOURCES:	Zacks, 2000		Buderi, 2000c

In the U.S. Pharmaceutical industry expenditures on R&D in 2000 represented 20.4% of sales (and $26.4 billion), up from 11.9% of sales in 1980 (or $1.5 billion; Noonan, 2000). Private firms now fund over $10 billion of health R&D (Shimm and Spece, 370). Commercial funding takes various forms: contracts, direct grants, consultancy fees, free equipment, expense paid trips to conventions--often at resorts--, and gifts, etc (Huth, 392f; Kingman, 1994; Fine, 1999; Shimm, Spece, and Di Gregorio). The first three also occur in government funding.

New drugs and vaccines represented about 70% of Biotechnology patents since 1996 (2842 of 5492; La Montagne, 2001: 1724).

In Canada, with R&D at 14.1% of revenue, an increase of 14.7% over the previous year, the pharmaceutical industry is the second most R&D intesive of all sectors (Re$earch Infosource, 2002).

Once discovered however new pharmaceuticals are relatively easy to copy, viz., as generics, thus leading to countless narrow patents which protect minor imitations of innovations, mostly by the threat of litigation—as seen in Apotex's numerous legal warnings to Dr. Olivieri ; indeed most technological and commercial innovation involves minor modifications of new systems, and often are more imitative than new (Freeman,).

To solve the problem of the underfunding of clinical research it has been argued that simple medical devices should be patented and the earnings applied to clinical research (J Rees); e.g., diagnostic tools such as the application of Tlo1 phototherapy originally used for psoriaisis to eczema and other related diseases. And Breslow's techniques for measuring the depth of a

melanoma tumor, are ‘conceivable as intellectual property and amenable to patenting,”, and the income generated should be used to supply more funds for clinical research (Rees, 2000). But, David Korn and Roger Meyer protest, this would only reinforce the current ‘epidemic of patenting an privatisation of fundamental and applied clinical knowledge which has always been in the public domain’; the conversionof newmedical knowledge to private property would threaten fundamental biodmedical research on which all future scientific advancements depend” (letter, *Lancet* 9 dec 2000; 2015). In effect they argue the key implication of the R, T & D continuum, namely that the common intellectual property right which scientific openness demands is incompatible with still further extension of private intellectual property rights appropriate to technology development and commercial products.

Patents cover gene fragments, DNA sequences, and perhaps even a full length gene (Doll, 1998). In 1980 for example the US Supreme Court approved the patenting of a genetically engineered life form, on the grounds that it represented a “human made invention” (Rifkin, 42f, 45f). Merck pharmaceuticals and the US National Institute of Health NIH are cooperating in allowing IH funded researchers to use patented transgenic animals like the oncomouse without obtaining approval of the firm owning the patent (Dupont on licence from Harvard University), funding patent-free transgenic mice for cancer research, liberating it from reliance on the oncomouse which was patented in 1988 (Marshall, 2000a, 2000b).

PRIVATE IP & PATENTS

Patents are one of the three main legal mechanisms for protecting private intellectual property (along with copyright and trade marks, neither of which will be discussed here).

PATENTS are a form of private intellectual property right, through which governments grant a monopoly of knowledge to a person or organization to “make, use, and sell a new device, design, or type of plant they have invented (cf . Whitbeck, 48). They represent a limited monopoly of knowledge, for one must also “make plain” (patent) full information about the nature and details of one’s invention. The monopoly is only for a specific pharmaceutical, not the medical treatment itself. That remains the common intellectual property of healthcare professionals.

Patents allow some openness, while also ensuring that innovators can reap a commercial reward for their intellectual work. They only last long enough to recover one’s investment in R&D. The US standard is 20 years for useful technologies like pharmaceuticals and 14 years for designs (Shulman, 2000).

It typically takes around US$600 mn to successfully bring a new drug to market (CMAJ, 2002). Patents are an appropriate legal mechanism for protecting and encouraging genuinely innovative technologies and products, such as new medical devices (surgical tools, bandages, etc) and drugs (e.g., T2 to D3); but they are in appropriate for scientific discoveries (R1 to R3), and especially not for life forms or the human body. US law assumes that “normal scientific and engineering work development process should be rewarded by a patent,” however minimal the novelty of the innovation, and similar to existing technologies and products (Barton, 2000). The confusion of research with technology and product development, and patent driven commercial and university funding of scientific research, and the high costs of patents, all result in the US

patent law acting to inhibit scientific research and technological innovation, in direct contradiction of its original intent. Accordingly there is much talk of patent reform:

The US Patent Office's requirements for a patent (utility, novelty and nonobviousness) may however be loosely defined (Barton, 2000). A novel application extension of a well known, widely published technique thus may be patentable. Broad patents may preempt broad areas of potential threaten scientific research, follow on research with commercial potential, such as bio technology and Computer software, research animals, gene sequencing / fragments, and research animals. The development of a new pharmaceuticals may involve negotiating numerous cross licences and agreements with firms that have patents on various steps in the research; thus patents inhibit open access by researchers to useful information and the research process itself.

European nations however have more restricted criteria, less lengthy periods of patent protection; and India allows the copying of pharmaceuticals patented in other nations. So patents represent only a partial, and variable, solution to the problems of intellectual property in commercially funded R&D. Unlike the US, European patent law allows for third party review of patent applications for 18 months prior to issuance of a patent, once the application is filed with the patent office, and for instance competing interests who might dispute a patent application have greater access to patent office prior to its granting, thus toughening and sharpening the case for a patent (Barton, 2000). There is a presumption of validity in US patent law which makes it difficult to declare a bad patent invalid.

Broad patents lead to errors, such as patents for pseudoscientific technologies such as cold fusion and psychic force detection systems. In patents, we need prior disclosure and more narrowly defined criteria (Barton, 2000). Outside the EU, patent applications do not automatically apply in other nations moreover, thus requiring applicants to apply in diverse jurisdictions, and raising the legal costs and barriers to innovative R&D even higher.

Patents raise many legal and financial barriers to innovative RT&D. The law strongly favours the holder of a patent, however invalid or mistaken its granting may have been. Indeed the costs of a patent application, c. $10000, and $1.5 mn to litigate a patent are rising rapidly and prohibitively. Patents are increasingly becoming a powerful legal weapon for firms to deploy against potential competitors, e.g., by developing enormous defensive patent portfolios.

New methods or processes are also patentable. And using a new technologies usually involves learning a new 'technique'. But the patenting of innovative methods is widely disputed. A comparison to patenting business methods, such as the notorious Amazon.com's 1 click shopping patent, which Jeff Bezos himself questions, may help. Problems with patents are manifold: the high cost of obtaining patents, and the litigation barriers to innovation they represent ( ). Also the vagueness of notions like 'prior art' in US patent law, inadequate prior discussion before granting a patent, are controverted ( )

Whether, or specific techniques for using various medical devices or technologies is a hotly disputed. The AMA agrees with patenting innovative medical technologies such as new types of surgical instruments, endoscopes, etc, but opposes as unethical patents for a new medical "technique, method or process performed as a necessary component of a surgical or medical procedure', administering surgical or medical therapies and making diagnoses (Garris,

1996: 101, 103; cf 86f, 94). openness is for the AMA a basic tenet of medical professionalism, for therapeutic knowledge should be widely shared and available as possible for the progress of science and the benefit of patients, mankind, patients (Garris, 1996; 89f, 93). The US patent office however grants about a dozen medical procedure patents each week It supports the patenting of a new technique only if it is a 'necessary component of a patentable machine or device.' (Garris, 1996: 85, 86). The benefits of patents, Garris argues, outweigh the costs (104) publicize the technical information, and the royalties charged for using a patented procedures would not only decline over time but lead to improvements in care that offset those costs (Garris, 98f) In effect the AMA ties a specific technique to the technology for which it is designed. This is a corollary of the distinction between scientific research and technological innovation latent in the R, T & D continuum.

We need to developing new patent laws, which allow for the free flow of information and still protect the intellectual property rights of those who p;ay for and conduct research" , and thus (continue to) have the best of both worlds (Gibbs, 1996). Raising the standards for patentability; decreasing the use of patents to inhibit scientific research; and making it easier for objectors to oppose invalid patents, or dubious patent applications (as in Europe). And providing :an automatic royalty free licence to use any patented technology in research;

RT&D: RESOLVING THE TENSIONS

The main competing interests involved in commercially funded pharmaceutical research are the scientists, the subjects of the research, the universities and research organizations in which scientists work, the pharmaceutical firms that sponsor the research, and the general public whose interest in the advancement of both their health and knowledge are served by such research.

The Gelsinger, Olivieri and Dong cases, among others constitute warnings that academic freedom needs vigilant protection and support, notably by the host institutions whose mandate it is to support research, universities, teaching hospitals and public regulatory authorities, and, I would add, by commercial firms whose own welfare depends on high quaqlity R, T & D, such as the many biotech and telecommunications electronics firms dotting the emerging knowledge economy. "We would like to believe that most universities would support faculty members who were exerting their right to academic freedom in the fact of an angry and disappointed industrial sponsor of trials that did not go their way," remark Nathan & weatherall (2002: 1370).

The main problems identified here, especially in the Gelsinger and Dong cases, are the threats against open communication by researchers, notably of adverse findings, to the scientific community, and in clinical research, of risk to patients and subjects of the research and the in adequate response of public host institutions such as universities and teaching hospitals, and public regulatory agencies—. The lack of on the part of host institution support for the academic freedom of researchers and core principles of medical ethics, along with their tolerance of conflict of interests is significant and worrying. High Tech commercial firms that are familiar with R&D should also know better, but at least one might say that, unlike the host public institutions of academic and clinical research, they are operating within their legitimate mandate as private enterprises, albeit without adequate recognition of their own interest in open research. When the public interest, e.g., in scientific integrity, academic freedom, and medical ethics is

not protected by Public institutions whose mandate it is to support and oversee these spheres, then a decline of public trust and credence in science, academics, and healthcare professionals is to be expected (along with a rise in faith in magic, superstition, and all manner of mythmaking and dubious panaceas, conspiracies, gurus, quacks, preachers, faith healers, and the whole panoply of ideological scam artists.

Much current R&D then involves competing interests, in scientific openness, financial and commercial funding, the professional advancement and personal ambition of the researchers, host institution support, and sometimes even ideological and religious biases (e.g., creationists researching evolution).

Following editorial style in the medical literature, I speak of competing rather than conflicting interests (Smith, 1994, 1998; Angell and Kassirer, 1996; Whitbeck, 78). For such interests reinforce as well as oppose each other. To talk only of interest conflicts is inaccurate, polarizing and tends to encourage overly critical judgement. Intellectual property problems moreover are usually not matters of intentional immorality or corruption. A researcher's interest in knowledge can furthermore represent competition to determine the truth, as when Watson and Crick raced against Linus Pauling to discover the DNA's double helix structure.

To resolve the ethical tensions / conflicting obligations raised by institutional social, cognitive and complexity of RT&D, especially when commercially funded, the following priorities.

In general, one should try to openly discuss and negotiate the terms of research support, in ways that reocngize and protect competing stakeholder interests: the subjects of clinical trials and others with similar medical conditions in health; researchers and relevant knowledge communities in scientific integrity and openness; commercial funding organizations and host institutions in recouping costs and realizing gains; host institutions, public regulatory agencies, and the relevant broader publics in seeing progress both in scientific knowledge, technological innovation, the quality of healthcare, and economic growth (Huth, 392f; Munthe and Welin, 1996; Moses, et al, 2002).

First, I suggest, should come the *Health* interest of those with the medical condition being studied (Lancet, 2000). All involved in clinical research should care for the subject's health. The scientists should openly communicate their research methods and findings. Funding sponsors furthermore have to recover their costs, and commercial sponsors need to develop profitable products. To sort these out however we need to understand the R&D continuum. The public demands acess to new treatments, the best products of biomedical R, T & D.

Third, come the *Economic* interests of funding organizations, public and commercial. They should be given adequate opportunity to recover their costs, and funding sponsors should be allowed to reap a reasonable return on their investment. Research partners like host institutions and governments should also share in the benefits, and rewards to the extent appropriate; and the researchers themselves should enjoy appropriate professional recognition.

Second, ensuring the integrity of scientific research is necessary, for it is a prerequisite of all the other interests involved, including that of the patients, researchers, host institutions, funding sponsors, clinicians and researchers. is evident (Lancet, 2002c).

The *Knowledge* interest of the scientific community, viz., in the integrity of research; for ascertaining the truth, viz., re a drug's safety or efficacy, is a prerequisite to achieving all other goals. To the extent that research findings are adverse, moreover, the findings must be published fully and as soon as possible. This is especially requisite where there are serious risks to patient health and the drugs in question might have to be withdrawn from use, as in the deferiprone, gene therapy and coagulate factor / blood donor cases.

Third, a related concern, is *disclosure of interests*, or openness about one's interests in the research, especially financial interests. The financial interests, of sponsoring organizations, public and private, researchers, and others are critical factors, for they have been shown to bias research, e.g., in support of a favourable rather than adverse findings about, e.g., the drug under trial (). One should not violate the openness ethic, viz., by imposing a private intellectual property right on scientific research (i.e., in R1 to R3), as happened in the Olivieri and Dong cases.

The first three considerations then militate in favour of openness. This brings us to the core tension around intellectual property. The health and knowledge interests, I note, favour openness and a common intellectual property right, while the economic interest calls for a private property approach.

Finally, the funding sponsor's interest in and a return on their investment is legitimate. Funding organizations have the right to recover their costs and a reasonable return on their investment. In this they resemble venture financiers, not the knowledge workers who actually produced the cognitive assets. At the very least all involved should have a real likelihood of recouping costs.

And commercial sponsors, should have real *opportunity* to reap some gain on their investments. Since both investment, like research, technology and product development, are all risky. Success is not assured in these, or most other human endeavours. So no guarantee of satisfactory gains on investments of time or money, for researchers, patients, universities, hospitals, government or commercial sponsors, can be promised. Only the opportunity should be there.

Given their superior financial performance, however, pharmaceutical firms can afford to invest patient capital over the long term and to resist short term demands for high returns; and they probably could also allow more open publication of the results of the research they support.

This is a real concern, for R&D is often an uncertain, lengthy and costly collaborative process. In many cases research fails to support the original hypotheses after years of effort and study, as we saw with L1. As a result there is little or nothing in the way of economic deliverables or, sometimes, professional advancement. Indeed only in a minority of cases does research yield levels of return on investment equal to what markets prefer. So professional and financial risks are a real concern for both researchers and funding organizations.

These four considerations represent guidelines for defining a solution space that at least respects the interests of all the competing interests involved in clinical RT&D. And there have been some interesting developments.

In spring 2001 the University of Toronto negotiated a new affiliation agreement with its teaching hospitals. It protects researcher's rights to disclose safety concerns to research subjects, forbids research sponsors from suppressing research results, limits publication delays to six months, and proposes a dispute resolution mechanism (Spurgeon, 1998).

In September, 2001 for instance the editors of the major medical journals have adopted a policy of full disclosure of interests by all contributors [International Committee of Medical Journal Editors. (2001). There is an emerging consensus that hospital research ethics committees should themselves ensure transparency about conflicts of interest and act with other host institutions to protect scientific integrity[Goldner. (2000). Any restriction of scientific openness, viz in commercially funded research, for instance, should be narrow, limited, and temporary, viz., only to the extent needed to insure recovery of all research costs, and, for commercial organizations, a reasonable return on their investment. While openness is required for quality and integrity in research, one might consider some limited compromises, on the assumption that formal agreements among research partners include a commitment by all parties to respect scientific openness, and patient rights, while seeking to advance knowledge and realize a return on their investments: communication with all or some members of the relevant knowledge community, host institutions, funding organizations, and other appropriate publics, and relatively short delays in the publication of findings as is done in some universities, e.g., up to a year.

Funding organizations might enjoy a priority right to first views of the results of research they funded. Access to research related information, such as raw data, may be partial and limited to some publics, for everyone does not need to know every piece of information about every research project. But deciding who has a right to know what when, etc., is difficult. This means ensuring the independence of the researchers, and the academic freedom of participating universities, e.g., to design and conduct research, and publish all data and results, however adverse. Where and to the extent appropriate, funding sponsor prepublication review and delays from 2 to 6 months, e.g., to allow for patent applications, could both be respected. All host institutions supporting clinical research, especially universities and hospitals, should support academic freedom and scientific openness, and resist threats to scientific integrity from research sponsors, private or public. Scientific openness and academic freedom, that is, must be respected.

One cannot here go into every permutation of all these options. Suffice it to say that without openness, scientific research will wither and die, and with it, the knowledge economy, especially the pharmaceutical industry. This is not a scenario anyone desires, least of all those with medical conditions that would benefit from new and better drugs and treatments. Only some such mutually acceptable arrangements can reduce the tensions raised by the social and cognitive complexity of RT&D in today's high tech knowledge economy. And reduce them, we must.

ABBREVIATIONS USED:

BMJ = *British Medical Association Journal*

JAMA = *Journal of the American Medical Association*

NEJM = *The New England Journal of Medicine*

SEE = *Science And Engineering Ethics*

TR = *Technology Review*

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